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PREVENTIVE HEALTH SYSTEMS INC FALLS CHURCH VA
CRYOBIOLOGICAL PRESERVATION OF BLOOD. (U)

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⑯ ⑯ ONR CONTRACT NO.
N00014-78-C-0611

⑯ ⑯ CRYOBILOGICAL PRESERVATION
OF BLOOD

⑯ ⑯ Progress Report

⑯ ⑯ Author: William Mercer-Daly, M.D.

⑯ ⑯ 11 21 Nov 78

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Submitted by:

Preventive Health Programs, Inc.
1500 Leesburg Pike, Suite 1500
Falls Church, Virginia 22041

November 21, 1978

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**PREVENTIVE
HEALTH
PROGRAMS**

a part of
PHP CORPORATION

5205 Leesburg Pike, Suite 1500 • Falls Church, Virginia 22041 • (703) 998-7808

November 21, 1978

Scientific Officer
Program Director, Biophysics
Biological Sciences Division
Office of Naval Research
800 North Quincy Street
Arlington, Virginia 22217

Attention: Dr. Arthur B. Callahan

Reference: ONR Contract No.: N00014-78-C-0611

Dear Sir:

This is the first of several progress reports, or what we feel might more appropriately be termed letters of review, submitted in compliance with contract data requirements (DD Form 1423).

Yours truly,

William Mercer-Daly, M.D.
Principal Investigator

PREVENTIVE HEALTH PROGRAMS, INC.
(Vice President & Medical Director)

WMD:cac

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Under the terms of the original contract (reference ONR contract number N00014-78-C-0611) Preventive Health Programs, Inc. (PHP) shall:

1. Review and evaluate the current status of existing programs in the United States and the United Kingdom on the cryobiological preservation of whole blood and blood components, with particular reference to the Armed Services.
2. Make recommendations based on the findings for future research and development of the cryogenic program.
3. Evaluate present and proposed techniques for cryo-preservation with particular reference to glycerol, hydroxy ethyl starch (HES) and polyvinylpyrrolidone (PVP).

It has rapidly become apparent that the task undertaken was more complex and multi-faceted than originally anticipated and this report will delineate: (i) what has been achieved to date, (ii) where we see the logical progression in the program, (iii) set the scene for the next phase of our investigation which will provide the material for progress report number two.

It is too early at this point in time to attempt to forecast how many progression reports will be submitted leading to our final conclusions, but it is felt that a minimum of three such will be required in order to cover the truly vast areas of research demanding attention.

It is interesting to note at this stage that PHP's role as an investigator, evaluator and assessor of priorities for further study has been accepted with enthusiasm by researchers and especially so in an area where academic conservatism and peer competitiveness tends to make free information exchange somewhat difficult. ONR's decision that an unbiased, non-partisan health organization be retained to undertake this task has already been fully justified by PHP's full acceptance by research organizations and their scientists throughout the United States and Europe.

To date, PHP has undertaken a literature search and acquisition program and has already developed the nucleus of a comprehensive data base at its headquarters in Falls Church, utilizing the resources of MEDLARS, Bio Abstracts, N.T.I.S., Defense Data Center (DDC) the N.I.H. medical reference library and the University of Georgetown Medical Library. We have already acquired a formidable nucleus for a bibliography which will be submitted in due course.

Leading researchers in the fields of blood research have been contacted and their encouragement and response in granting interviews and in providing up-to-date information and papers is greatly appreciated by our investigative team.

These contracts have not, of course, been confined to the United States. Authorities in the United Kingdom and Europe have been approached regarding our program and details for literature acquisition and personal contact are being developed and will be the subject of our continuing reports.

Appointments and interviews with leaders in the field of cryobiological and allied research that have already taken place include such authorities as Dr. Aaron Kellner, Director at N.Y. Blood Center; Dr. A. Rowe, N.Y. Blood Center; Dr. M. Merryman, American Red Cross Blood Research Program; Dr. C. Schaffer, Baltimore Cancer Research Center; Dr. David Aminoff, Memorial Institute, University of Michigan; Dr. R. Valeri, U.S. Naval Blood Research Program; Dr. C. Huggins, Manhattan General Hospital, et al.

In the United Kingdom arrangements are being made to meet with workers from the Army Blood Supply Depot at Aldershot, the Medical Research Council in London, the University of Southampton and University of Leeds. These target areas will be visited by Dr. William Mercer-Daly, the principal investigator for PHP in the near future. Dr. Mercer-Daly will also make a liaison visit with the Director General, Royal Army Medical Corps, Sir Richard P. Bradshaw, Q.H.P., M.R.C.S., L.R.C.P., F.R.C., Path., M.F.C.M., D.T.M.&H. and his staff to further coordinate and integrate our interservice relationships.

The services of a Research Assistant have been engaged to assist with the undertaking. She is already engaged in an intensive literature search in the United Kingdom, where she lives, and coordinates PHP's international effort. This lady has worked in the area of blood research for many years and offers to the project an in-depth understanding of the problems as well as a most positive approach as to their solution. We were indeed fortunate in obtaining her assistance.

As my research assistant, she recently attended the Conference on Platelet Preservation by Freezing, October 25 and 26, 1978, sponsored by the D.C. Chapter of the American Red Cross in Washington, D.C. A technical report on the highlights of the conference will be included in our next report.

It is felt that the mission with which PHP has been charged has gotten off to an excellent start not only in developing an in-depth review and acquisition of material relating to the subject of blood preservation, but in establishing a rapport and working relationship with the principal researchers in the United States and the United Kingdom.

At this stage it would be premature to offer any firm conclusions as to where current research is leading, but certain areas of interest rather tend to highlight themselves and definitely appear to be worthy of further and more in-depth scrutiny. These include:

1. Biosynthesis of blood group substances leading ultimately to the development of a Universal Blood.
2. Cryoinjury and cryoprotection programs and techniques.
3. Platelet preservation. Little has changed over the years in this area of research.
4. Plasma expanders and synthetic fluorocarbons for utilization in emergency situations and prior to the administration of red cells.
5. White cell preservation, its complexities and its potentials.
6. The development of a Megamolecule of Haemoglobin with a lifetime of 36 hours or more.
7. The role of bone marrow and its place in the total picture of blood research.

PHP will be closely observing these and other research areas and will report on each as separate items in future progress reports.

In the area of plasma expanders and their utilization, it would appear to be the consensus of opinion that PVP (Polyvinylpyrrolidone) has little if any role to play in the future. The tissue storage of the molecule has caused concern and, although no actual cases have been proven, there is a suspicion that the substance is potentially carcinogenic. An NIH study did apparently identify PVP as a causitive factor in causing cancer in a rat and the FDA is closely looking at the substance. HES is of course, another story as it is biodegradable and some authorities see a promising future for HES, perhaps utilized in a glycerol combination. As for glycerol itself a great deal of progress has been made using different concentrations. For instance, New York Blood Center uses low concentrations, whereas American Red Cross Blood Research Lab

uses high concentrations. Comparison and evaluation studies here should prove interesting.

A great deal of time, expertise, financial support and energy has gone into the blood program world-wide and very significant progress has been made in many areas of research. There does, however, still remain a great deal to be done and we at Preventive Health Programs see our role to be that of coordination, cooperation and liaison and in acting as a catalyst and point of focus in drawing together widely scattered and diverse agencies in developing a unified international program for the benefit of mankind.

End of Report